7.0 CLAIMS

CLAIMS:

5   1.   A method for detecting tamoxifen-resistant breast cancer cells, comprising:

        a)   obtaining a sample suspected of containing tamoxifen-resistant breast cancer cells;

10   b)   contacting said sample with an antibody that specifically binds to a polypeptide selected from the group consisting of tyrosine protein kinase receptor (TIE-2), endothelin-1 receptor (EDNRA), transforming growth factor β3 (TGFβ3), transforming growth factor receptor βIII (TGFRβIII), vascular permeability factor receptor (VEGFR1), vascular endothelin growth factor (VEGF) and basic fibroblast

15   growth factor receptor (bFGFR) under conditions effective to bind said antibody and form a complex;

        c)   measuring the amount of said polypeptide present in said sample by quantitating the amount of said complex; and

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        d)   comparing the amount of polypeptide present in said sample with the amount of polypeptide in estrogen-stimulated, tamoxifen-sensitive and tamoxifen-resistant breast cancer cells, wherein an increase in the amount of TIE-2, EDNRA, TGFβ3, TGFRβIII, VEGF or VEGFR1 polypeptide or a decrease in the amount of

25   bFGFR polypeptide in said sample compared with the amount in estrogen-stimulated or tamoxifen-sensitive breast cancer cells indicates the presence of tamoxifen-resistant breast cancer cells.

        2.   The method of claim 1, further comprising:

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a)   measuring the amounts of two or more polypeptides selected from the group consisting of TIE-2, EDNRA,   TGFβ3, TGFRβIII, VEGFR1, VEGF and bFGFR; and

5   b)   for each polypeptide, comparing the amount of said polypeptide present in said sample with the amount of the same polypeptide present in estrogen-stimulated, tamoxifen-sensitive and tamoxifen-resistant breast cancer cells.

3.   The method of claims 1 or 2, further comprising providing a diagnosis of

10   tamoxifen-sensitive or tamoxifen-resistant breast cancer.

4.   The method of claims 1 or 2, further comprising providing a prediction of the existence or development of tamoxifen-resistant breast cancer.

15   5.   A method of determining survival for an individual with breast cancer, comprising determining the levels of TIE-2, EDNRA, TGFβ3, TGFRβIII, VEGFR1, VEGF or bFGFR polypeptide in a breast cancer tissue sample from said individual, wherein the presence of elevated levels of TIE-2, EDNRA, TGFβ3, TGFRβIII, VEGF or VEGFR1 polypeptide or decreased levels of bFGFR polypeptide in said tissue

20   sample relative to estrogen-stimulated or tamoxifen sensitive breast cancer samples is associated with a decreased survival of the individual.

6.   A method for detecting tamoxifen-resistant breast cancer cells, comprising:

25   a)   isolating a nucleic acid from a sample suspected of containing tamoxifen-resistant breast cancer cells;

b)   contacting said nucleic acid with a pair of primers effective to amplify the nucleic acid sequences of TIE-2, EDNRA, TGFβ3, TGFRβIII, VEGFR1, VEGF

30   or bFGFR;

c)   amplifying said nucleic acid using said primers to form an amplification product;

d)   quantitating the amount of said amplification product formed; and

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e)   comparing the amount of said amplification product formed from said sample with the amount of amplification product formed under identical conditions from estrogen-stimulated, tamoxifen-sensitive and tamoxifen-resistant breast cancer cells, wherein a difference in the amount of said amplification product formed from

10   said sample compared with the amount formed from estrogen-stimulated or tamoxifen-sensitive breast cancer cells indicates the presence of tamoxifen-resistant breast cancer cells.

7.   The method of claim 6, further comprising:

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a)   measuring the amount of two or more amplification products using primers effective to amplify the nucleic acid sequences of TIE-2, EDNRA, TGFβ3, TGFRβIII, VEGFR1, VEGF or bFGFR; and

20   b)   for each amplification product, comparing the amount of amplification product formed from said sample with the amount of amplification product formed from estrogen-stimulated, tamoxifen-sensitive and tamoxifen-resistant breast cancer cells.

25   8.   The method of claim 6 or 7 further comprising providing a diagnosis of tamoxifen-sensitive or tamoxifen-resistant breast cancer.

9.   The method of claim 6 or 7 further comprising providing a prediction for likelihood of development of tamoxifen-resistant breast cancer and subsequent patient

30   survival.

10. A method of determining survival for an individual with breast cancer, comprising determining the levels of TIE-2, EDNRA, TGFβ3, TGFRβIII, VEGFR1, VEGF or bFGFR amplification product formed from a breast cancer tissue sample from said individual, wherein the presence of elevated levels of TIE-2, EDNRA, TGFβ3, TGFRβIII, VEGF or VEGFR1 amplification product or decreased levels of bFGFR amplification product formed from said tissue sample compared with estrogen-stimulated or tamoxifen-sensitive breast cancer cells is associated with a decreased survival of the individual.

11. A method for altering the phenotype of a breast cancer cell comprising contacting the cell with (i) a gene selected from the group consisting of TIE-2, EDNRA, TGFβ3, TGFRβIII, VEGFR1, VEGF and bFGFR and (ii) a promoter active in said cancer cell, wherein said promoter is operably linked to the region encoding said gene, under conditions effective for the uptake and expression of said gene by said breast cancer cell.

12. A method for treating breast cancer, comprising:

a)   providing an effective amount of an antiangiogenic agent; and

b)   providing an effective amount of tamoxifen.

13.   The method of claim 12, wherein the antiangiogenic agent is selected from the group consisting of AGM-1470 (TNP-470), platelet factor 4 and angiostatin.

14.   A method for treating breast cancer, comprising:

a)   providing an effective amount of an antisense construct containing a gene selected from the group consisting of TIE-2, EDNRA, TGFβ3, TGFRβIII, VEGF and VEGFR1 under conditions allowing for the uptake and expression of said construct by said breast cancer; and

b)   providing an effective amount of tamoxifen.

15.   A method for treating breast cancer, comprising:

a)   providing an effective amount of an expression construct containing a gene encoding bFGFR under conditions allowing for the uptake and expression of said construct by said breast cancer; and

b)   providing an effective amount of tamoxifen.

16.   A kit comprising:

a)   one or more antibodies that specifically bind to TIE-2, EDNRA, TGFβ3, TGFRβIII, VEGFR1, VEGF or bFGFR polypeptide; and

b)   a container for each of said antibodies.

17.   A kit comprising:

a)   one or more pairs of primers effective to amplify the nucleic acid sequences of messenger RNAs encoded by TIE-2, EDNRA, TGFβ3, TGFRβIII, VEGFR1, VEGF or bFGFR; and

b)   a container for each of said primers.

18.   A method of detecting markers for tamoxifen-resistant breast cancer, comprising:

a)   isolating nucleic acids from samples of estrogen-stimulated, tamoxifen-sensitive and tamoxifen-resistant breast cancers;

b)   converting messenger RNAs to cDNAs;

c)   screening the cDNA species with a human cDNA expression array; and

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d)   identifying cDNA species that are differentially expressed in tamoxifen resistant breast cancers *versus* estrogen-stimulated or tamoxifen sensitive breast cancers, wherein differential expression indicates a marker for tamoxifen-resistant breast cancer.

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19.   A pharmaceutical composition comprising two or more nucleic acids selected from the group consisting of TIE-2, EDNRA, TGFβ3, TGFRβIII, VEGFR1, VEGF and bFGFR.

15   20.   The composition of claim 19, wherein said nucleic acids are in the form of vectors.

21.   A pharmaceutical composition comprising two or more polypeptides selected from the group consisting of TIE-2, EDNRA, TGFβ3, TGFRβIII, VEGFR1, VEGF
20   and bFGFR.